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| 09/806,287 | 03/28/2001 | Young-Ro Byun | 55761 | 6676 |

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|---|---|
| WARE, TODD | |
| **ART UNIT** | **PAPER NUMBER** |
| 1615 | |

DATE MAILED: 07/30/2002 3

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/806,287 | Applicant(s) BYUN ET AL. | |
|---|---|---|---|
| | Examiner Todd D Ware | Art Unit 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Receipt of papers filed 3-28-01 is acknowledged. It is noted that claim 9 recites "acute promyelocytic leukemia" twice. Deletion of one occurrence is requested.

### *Claim Objections*

1. Claim 5 is objected to because of the following informalities: claim 5 depends from itself. Appropriate correction is required.

2. Claims 8-10 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

3. Claim 8 is objected to because of the following informalities: claim 8 has abbreviations in the claims where no definition in a parent claim is provided. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of head and neck cancer, skin cancer, lung cancer, breast cancer, cervical cancer, bladder cancer, and promyelocytic leukemia, does not reasonably provide enablement for other conditions yet to be

discovered to be treatable with retinoic acid administration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines a patient in need of retinoic acid administration. While applicant has set forth certain conditions treatable with retinoic acid, the scope of the claim is not limited to these conditions in that it encompasses conditions/diseases yet to be discovered treatable with retinoic acid administration. The guidance and working examples provided by the specification is directed toward making

a retinoic acid controlled release formulation and includes reference to the use of retinoic acid for treatment of various types of cancer. However, the amount of guidance to determine whether a particular condition not disclosed by the instant specification is lacking. No criteria nor direction for determining likelihood of relief for a condition is provided (i.e. no mechanism of action for the agent or common mode/factors of condition or disease progression are presented). The skilled practitioner would first turn to the instant specification for guidance in using the compositions for treating a condition/disease with retinoic acid, as claimed. However, the specification does not provide sufficient guidance for using retinoic acid compositions, as claimed. As such, the skilled practitioner would turn to the prior art for such guidance. However, even though the skill level of those in the art is high, the prior art does not provide predictability for conditions capable of being treated with retinoic acid. Finally, the practitioner would turn to trial and error experimentation to use retinoic acid, without guidance from the specification or the prior art. Therefore, undue experimentation becomes the burden of the practitioner.

6. Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim does not comply with the written description requirement for the reasons set forth previously with respect to the 35 U.S.C. 112, first paragraph, scope of enablement rejection (paragraph 5). Most

notably, the claimed method requires treatment of an unspecified condition. One skilled in the art would conclude that the artisan was not in possession of the claimed method of use.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 9-10 provide for the use of a drug release system, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

***Claim Rejections - 35 USC § 101***

10. Claims 9-10 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gref et al (5,543,158; hereafter '158) in view of Rodgers et al (5,534,261; hereafter '261).

14. '158 teaches controlled release microsphere in which biodegradable polymer and the instant amphoteric block copolymer are mixed and an active agent is incorporated into the microsphere. The ratios of biodegradable polymer/block copolymer and active agent/microsphere are within the instant ratios. These microspheres are not rapidly cleared from the blood stream by the macrophages of the reticuloendothelial system. '158 also teaches that biologically active molecules are contemplated to be delivered but does not teach that the active agent is retinoic acid.

15. '261 is relied upon for teaching controlled release microspheres made of polymers for controlled delivery of retinoids.

16. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to incorporate a retinoid into the formulation of '158 with the motivation of providing a delivery formulation for a retinoid that is not rapidly cleared from the blood stream by the macrophages of the reticuloendothelial system.

17. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cha et al (WO 97/15287; hereafter '287) in combination with Rodgers et al (5,534,261; hereafter '261) and further in combination with Lippman et al (1992).

18. '287 teaches biodegradable polymeric microspheres that provide controlled release of an active agent. These microspheres comprise the instant amphoteric block copolymer mixed with interferon-α. '287 does not teach delivery of retinoic acid with the instant microspheres.

19. '261 is relied upon for all that it teaches as stated previously.

20. Lippman is relied upon for teaching co-administration of interferon-α and 13-cis-retinoic acid for treatment of squamous cell carcinoma of the cervix.

21. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to administer retinoic acid in combination with the interferon-α of '287 with the motivation of providing a controlled release formulation for treating squamous cell carcinoma of the cervix.

22. Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cha et al (5,665,428; hereafter '428) in combination with Rodgers et al (5,534,261; hereafter '261) and further in combination with Lippman et al (1992).

23. '428 teaches biodegradable polymeric microspheres that provide controlled release of an active agent. These microspheres comprise the instant amphoteric block copolymer mixed with interferon. '287 does not teach delivery of retinoic acid with the instant microspheres.

24. '261 and Lippman are relied upon for all that they teach as stated previously.

25. Accordingly, it would have been obvious to one skilled in the art at the time of the invention to administer retinoic acid in combination with the interferon-$\alpha$ of '428 with the motivation of providing a controlled release formulation for treating squamous cell carcinoma of the cervix.

***Conclusion***

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on M-F, 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703)308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

tw
July 27, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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